AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior listings, and versions, of claims in the application.

Listing of Claims

1. (previously presented) A method comprising:

1) screening a plurality of compounds for potential development as ~~a~~ candidate cognitive enhancer compounds by

2) determining the ability of said compounds to enhance cyclic adenosine monophosphate (cAMP) response element binding protein (CREB) pathway function wherein said screening and determining comprises the steps of:

a) contacting host cells comprising an indicator gene operably linked to a cAMP response element (CRE) promoter with a test compound and with a suboptimal dose of a CREB function stimulating agent simultaneously or sequentially, wherein said CREB function stimulating agent is forskolin;

b) determining indicator activity in said host cells which have been contacted with said test compound and with said CREB function stimulating agent, wherein said CREB function stimulating agent is forskolin;

c) determining indicator activity in said host cells which have been contacted with said CREB function stimulating agent alone, wherein said CREB function stimulating agent is forskolin;

d) determining indicator activity in said host cells which have been contacted with said test compound alone; and

e) determining indicator activity in said host cells which have not been contacted with said test compound or said CREB function stimulating agent, wherein said CREB function stimulating agent is forskolin;

f) comparing the indicator activity determined in each of steps b) through e)

g) selecting said test compound if:

i) the indicator activity determined in step b) is significantly increased relative to the indicator activity determined in step c); and

ii) the indicator activity determined in step d) is not significantly different relative to the indicator activity determined in step e);

h) repeating steps a) to g) with a range of different concentrations of said test compound selected in step g); and

i) selecting said test compound if:

i) the indicator activity determined in step b) is significantly increased relative to the indicator activity determined in step c); and

ii) the indicator activity determined in step d) is not significantly different relative to the indicator activity determined in step e) in the range of different concentrations of said test compound, and

3) identifying said test compound as a candidate cognitive enhancer compound if said test compound is selected in steps g) and i).

2. (original) The method of claim 1 wherein said host cells are contacted with said test compound prior to contact with said CREB function stimulating agent, wherein said CREB function stimulating agent is forskolin.

3. (original) The method of claim 1 wherein said host cells are human neuroblastoma cells.

4. (original) The method of claim 1 wherein said indicator gene encodes luciferase.

5. (cancelled)

6. (previously presented) The method of claim 4 wherein steps a) to g) are repeated with a range of four different concentrations of the said test compound selected in step g).

7. (currently amended) The method of claim 1 further comprising the steps of:

j) contacting cells of neural origin with said identified candidate cognitive enhancer compound and with a suboptimal dose of a CREB function stimulating agent simultaneously or sequentially, wherein said cells of neural origin are different from the host cells of step a) and wherein said CREB function stimulating agent is forskolin;

k) assessing endogenous CREB-dependent gene expression in said cells of neural origin which have been contacted with said candidate cognitive enhancer compound and with said CREB function stimulating agent, wherein said CREB function stimulating agent is forskolin;

l) assessing endogenous CREB-dependent gene expression in said cells of neural origin which have been contacted with said CREB function stimulating agent alone, wherein said CREB function stimulating agent is forskolin; and

m) comparing endogenous CREB-dependent gene expression assessed in steps k) and l), wherein a significant increase ~~difference~~ in the endogenous CREB-dependent gene expression in step k) compared to the endogenous CREB-dependent gene expression in step l) confirms that said compound is a candidate cognitive enhancer compound, thereby identifying said cognitive enhancer compound as a confirmed candidate cognitive enhancer compound.

8. (previously presented) The method of claim 7 wherein said cells of neural original are contacted with said candidate cognitive enhancer compound prior to contact with said CREB function stimulating agent, wherein said CREB function stimulating agent is forskolin.

9. (original) The method of claim 7 wherein said cells of neural origin are neurons.

10. (original) The method of claim 9 wherein said neurons are primary hippocampal cells.

11. (cancelled)

12. (previously presented) A method comprising

1) screening a plurality of candidate cognitive enhancer compounds by

a) contacting cells of neural origin with a candidate cognitive enhancer compound and with a suboptimal dose of a cyclic adenosine monophosphate (cAMP) response element binding protein (CREB) function stimulating agent simultaneously or sequentially, wherein said CREB function stimulating agent is forskolin;

b) assessing endogenous CREB-dependent gene expression in said cells of neural origin which have been contacted with said cognitive enhancer compound and with said CREB function stimulating agent, wherein said CREB function stimulating agent is forskolin;

c) assessing endogenous CREB-dependent gene expression in said cells of neural origin which have been contacted with said CREB function stimulating agent alone, wherein said CREB function stimulating agent is forskolin;

d) comparing endogenous CREB-dependent gene expression assessed in step b) with endogenous CREB-dependent gene expression assessed in step c);

2) identifying candidate cognitive enhancer compounds for further study as a cognitive enhancer if said endogenous CREB-dependent gene expression in step b) is significantly increased relative to said endogenous CREB-dependent gene expression in step c).

13. (previously presented) The method of claim 12 wherein said cells of neural origin are contacted with said candidate cognitive enhancer compound prior to contact with said CREB function stimulating agent, wherein said CREB function stimulating agent is forskolin.

14. (original) The method of claim 12 wherein said cells of neural origin are neurons.

15. (original) The method of claim 14 wherein said neurons are primary hippocampal cells.

16. (cancelled)

17. (withdrawn) A method for assessing the effect on long term memory formation in an animal of a candidate compound for enhancing CREB pathway function comprising the steps of:

a) administering said candidate compound to be assessed to said animal;

b) training said animal administered said compound under conditions appropriate to produce long term memory formation in said animal;

c) assessing long term memory formation in said animal trained in step b); and

d) comparing long term memory formation assessed in step c) with long term memory formation produced in the control animal to which said candidate compound has not been administered.

18. (withdrawn) The method of claim 17 wherein said mammal is a mammal

19. (previously presented) A method comprising

1) screening a plurality of compounds for potential use as a cognitive enhancer by assessing said compounds' ability to enhance cyclic adenonsine monophosphate (cAMP) response element binding protein (CREB) pathway function comprising the steps of:

a) contacting host cells comprising an indicator gene operably linked to a cAMP response element (CRE) promoter with a test compound, thereby producing a test sample;

b) contacting the test sample produced in step a) with a suboptimal dose of a CREB function stimulating agent wherein said CREB function stimulating agent is forskolin;

c) determining indicator activity in said host cells which have been contacted with said test compound and with said CREB function stimulating agent, wherein said CREB function stimulating agent is forskolin;

d) determining indicator activity in said host cells which have been contacted with said CREB function stimulating agent alone, wherein said CREB function stimulating agent is forskolin;

e) determining indicator activity in said host cells which have been contacted with said test compound alone; and

f) determining indicator activity in said host cells which have not been contacted with said test compound or with said CREB function stimulating agent, wherein said CREB function stimulating agent is forskolin;

g) comparing the indicator activity determined in each of steps c) through f);

h) selecting said test compound if:

i) the indicator activity determined in step c) is significantly increased relative to the indicator activity determined in step d); and

ii) the indicator activity determined in step e) is not significantly different than the indicator activity determined in step f);

i) repeating steps a) to g) with a range of different concentrations of said test compound selected in step h);

j) selecting said test compound as a candidate if:

i) the indicator activity determined in step c) is significantly increased relative to the indicator activity determined in step d) in the range of different concentrations of said test compound; and

ii) the indicator activity determined in step e) is not significantly different than the indicator activity determined in step f) in the range of different concentrations of said test compound;

k) contacting cells of neural origin with said candidate compound selected in step j) and with a suboptimal dose of a CREB function stimulating agent, wherein said CREB function stimulating agent is forskolin;

l) assessing endogenous CREB-dependent gene expression in the cells of neural origin which have been contacted with said candidate compound and with said CREB function stimulating agent, wherein said CREB function stimulating agent is forskolin;

m) assessing endogenous CREB-dependent gene expression in the cells of neural origin which have been contacted with said CREB function stimulating agent alone, wherein said CREB function stimulating agent is forskolin;

n) assessing endogenous CREB-dependent gene expression in the cells of neural origin which have been contacted with said cognitive enhancer compound alone;

o) assessing endogenous CREB-dependent gene expression in the cells of neural origin which have not been contacted with said CREB function stimulating agent, wherein said CREB function stimulating agent is forskolin, or with said cognitive enhancer compound

p) comparing endogenous CREB-dependent gene expression assessed in each of steps l)-o);

q) selecting said candidate compound if:

i) endogenous CREB-dependent gene expression assessed in step l) is significantly increased relative to endogenous CREB-dependent gene expression assessed in step m); and

ii) endogenous CREB-dependent gene expression assessed in step n) is not significantly different relative to the endogenous CREB-dependent gene expression assessed in step o);

2) identifying said candidate cognitive enhancer compound as a confirmed candidate cognitive enhancer compound if said compound is selected in steps h), j), and q).

20. (original) The method of claim 19 wherein said host cells are human neuroblastoma cells and said cells of neural origin are neurons.

21. (original) The method of claim 20 wherein said neurons are primary hippocampal cells.

22. (original) The method of claim 19 wherein said indicator gene encodes luciferase.

23. (cancelled)

24. (previously presented) The method of claim 19 wherein steps a) to h) are repeated with a range of four different concentrations of said test compound selected in step h).

25. (withdrawn) The method of claim 19 wherein said animal is a mammal.